

Application No. 10/534,079  
Paper Dated: September 27, 2010  
In Reply to USPTO Correspondence of May 25, 2010  
Attorney Docket No. 0470-051409

**AMENDMENTS TO THE CLAIMS**

This listing of claims will replace all prior versions, and listings, of claims in the application.

**Listing of Claims**

Claims 1-31 (Cancelled)

Claim 32 (Currently Amended) A process for the preparation of estra-1,3,5(10)-trien-3,15 $\alpha$ , 16 $\alpha$ , 17 $\beta$ -tetraol (1), comprising the steps of:

- 1) converting estrone (7) into 3-A-oxy-estra-1,3,5(10), 15-tetraen-17-one (6), wherein A is a protecting group;
- 2) reduction of the 17-keto group of 3-A-oxy-estra-1,3,5(10), 15-tetraen-17-one (6) to 3-A-oxy-estra-1,3,5(10), 15-tetraen-17 $\beta$ -ol (5);
- 3) protection of the 17-OH group of 3-A-oxy-estra-1,3,5(10), 15-tetraen-17 $\beta$ -ol (5) to 3-A-oxy-17-C<sub>p</sub>-oxy-estra-1,3,5(10), 15-tetraene (4), wherein C<sub>p</sub> is a protecting group;
- 4) oxidizing the carbon-carbon double bond of ring D of 3-A-oxy-17-C<sub>p</sub>-oxy-estra-1,3,5(10), 15-tetraene (4) to protected estetrol (3); and
- 5) removing the protecting groups, wherein protecting group A is removed first to form 17-OC<sub>p</sub> protected estetrol (2) and subsequently protecting group C<sub>p</sub> is removed to form estetrol (1);

wherein the protecting group A is selected from the group consisting of a C<sub>1</sub>-C<sub>5</sub> alkyl group and a C<sub>7</sub>-C<sub>12</sub> benzylic group and the protecting group C<sub>p</sub> is selected from monofunctional aliphatic hydroxyl protecting groups.

Claim 33 (Previously Presented) The process according to claim 32, wherein the protecting group is a C<sub>7</sub>-C<sub>12</sub> benzylic group.

Claim 34 (Previously Presented) The process according to claim 32, wherein the protecting group is a benzyl group.

Claim 35 (Cancelled).

Claim 36 (Currently Amended) The process according to claim 3532, wherein the monofunctional aliphatic hydroxyl protecting group is acetyl.

Claim 37 (Previously Presented) The process according to claim 32, wherein the reduction of the carbonyl group is carried out using a reducing agent selected from the group of metal hydride compounds.

Claim 38 (Previously Presented) The process according to claim 37, wherein the metal hydride compound is selected from the group consisting of LiAlH<sub>4</sub>, NaBH<sub>4</sub>, NaBH(OAc)<sub>3</sub>, ZnBH<sub>4</sub>, and NaBH<sub>4</sub>/CeCl<sub>3</sub>.

Claim 39 (Previously Presented) The process according to claim 38, wherein the metal hydride compound is NaBH<sub>4</sub> in combination with CeCl<sub>3</sub> hydrate.

Claim 40 (Previously Presented) The process according to claim 32, wherein the oxidation of the carbon-carbon doubly bond in ring D is carried out with an oxidizing agent comprising osmium tetroxide.

Claim 41 (Currently Amended) The process according to claim 40, wherein the oxidizing agent is osmium tetroxide immobilized on polyvinylpyridine (PVP) (OsO<sub>4</sub>-PVP).

Claim 42 (Currently Amended) The process according to claim 32, wherein the oxidization of the carbon-carbon double bond in ring D is carried out with a catalytic amount of OsO<sub>4</sub>-polyvinylpyridine (PVP).

Claim 43 (Previously Presented) The process according to claim 42, wherein the OsO<sub>4</sub>-PVP is used in combination with a co-oxidant.

Claim 44 (Previously Presented) The process according to claim 43, wherein the co-oxidant is selected from the group consisting of trimethylamine-N-oxide, N-methyl morpholine-N-oxide and hydrogen peroxide.

Claim 45 (Previously Presented) The process according to claim 44,

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wherein the co-oxidant is trimethylamine-N-oxide.

Claim 46 (Previously Presented) The process according to claim 32,  
wherein the protective C<sub>7</sub>-C<sub>12</sub> benzylic group is removed by catalytic hydrogenation conditions.

Claim 47 (Previously Presented) The process according to claim 46,  
wherein the catalytic hydrogenation conditions comprise a hydrogenation reaction using Pd on  
activated carbon under a hydrogen atmosphere.

Claim 48 (Previously Presented) The process according to claim 32,  
wherein the protective C<sub>1</sub>-C<sub>5</sub> alkyl group is removed by using BBr<sub>3</sub>.